Engineered Biomaterials Engineering Research Center

University of Washington

Evolving synthetic materials that actively turn on healing and exploit biological recognition and specificity

A National Science Foundation Engineering Research Center since 1996

Biomaterials and medical devices are widely used in human applications as diverse as heart valves, hip joints, pacemakers, tooth implants, drainage shunts, intraocular lenses, and heart-assisted devices. They save lives, improve the quality of life for millions, and form the basis for a strong, successful, humanitarian industry. But these biomaterials and devices never work as well as the part they are intended to replace. This leads to patient dissatisfaction, physician concern, and a financial burden on the health care system. The University of Washington Engineered Biomaterials (UWEB) Engineering Research Center (ERC) has a sharply focused objective: to develop a new generation of biomaterials that exploits specific biological recognition mechanisms. These materials will be designed so that upon implantation they will heal in the body in a facile, physiologically normal manner. They will function by interacting with specific cell receptors and initiating the desired biological responses. This is in contrast to existing biomaterials that are not recognized by the body and are walled off from it. By making materials with surfaces providing recognition sites, the UWEB goal will be achieved and nonspecific interactions will be minimized.

UWEB materials will find wide application in medicine and biotechnology and will allow the physician to control healing. The realization of biomaterials that heal is feasible at this time because of intellectual and technological advances in molecular biology, cell biology, and materials. In recent years, the most important advance has been in the detailed knowledge that biology is controlled through specific receptor mechanisms that turn signaling events on and off. The biochemical signaling agents direct subsequent reactions and healing. If we engineer biomaterial surfaces to resemble the natural triggers to specific cell-surface receptor sites, we can control cell signaling and the response of the organism to the implanted material. This will also permit improved medical diagnostics, robust biosensors, advanced cell culture for manufacturing biologicals, and enhanced methods for biomolecule purification. The paradigm of “learning from nature” that drives UWEB has profound implications for interdisciplinary research, new engineering concepts, novel education programs, the creation of research and development employment opportunities, and industrial competitiveness—not to mention saving lives and improving the quality of life for millions.

A sample is loaded into the vacuum chamber of an electron spectroscopy for chemical analysis apparatus to study its surface composition (graduate student, Mark Takeno, and UWEB Director, Buddy Ratner).

Research

UWEB is organized around three research thrusts:

- *Molecularly engineered materials*
- *Fundamental biology of healing and biointeraction*
- *Medical/biological studies of healing in cardiovascular sites, skin, bone, nerve, the eye, and diabetes*.

The following fundamental research ideas drive the UWEB program:

- The basic biology of normal healing and reconstruction must be understood in order to develop hypotheses for the control of healing by materials.
- Nonspecific reactions at the material surface must be inhibited; nature does not use nonspecific mechanisms.
- Cell physiology at surfaces must be accurately controlled by receptor interactions and biomechanics.
- Recognition sites or mimics of those sites, identified through studies of the basic biology of healing, must be precisely immobilized to the surfaces of medical materials.
- Cell culture models and implantation trials will test-out new materials that turn on normal healing.
- Viable manufacturing strategies must be developed to commercialize recognition materials.

Over 25 University of Washington lead investigators from the engineering, basic sciences, and medicine departments will collaborate with UWEB corporate partners, using a number of research approaches to

engineer biomaterials that heal. Computer-based molecular modeling will be used to design surfaces, and creative organic chemistry and genetic engineering will be applied to fabricate recognition sites. Self-assembly strategies can organize synthetic recognition sites at surfaces and define the relationships between specific cell-surface receptor activators. The UWEB program places special focus on cytokine production and on mapping the relationships between specific cytokine signals and consequent healing events.

Materials produced in the UWEB ERC will go directly to collaborating clinical investigators, who will study them as potential prosthetic materials and devices for skin, cardiovascular, bone, ophthalmologic, and neural sites. The ERC will address issues of healing, including healing templates for large-area wounds, percutaneous connections for prosthetic limbs, long-term implantable glucose sensors, small-diameter vascular grafts, and cochlear implants. Other applications for biomaterial surfaces with specific ligands include contact lenses, affinity chromatography, biosensors, nonfouling surfaces, and cell-culture substrates. Advances in the biology of inflammation and healing are also anticipated.

Education

The highly interdisciplinary UWEB program intrinsically offers opportunities for exploring new ideas in education at all levels. Fundamentals of modern cell and molecular biology will be taught to engineering undergraduate and graduate students and to our industrial collaborators. Specific topics will be offered to senior undergraduate and graduate students in receptor biology, cell signaling, cytokine production, healing, surface science, surface engineering, and self-assembly. General information on the elegance of modern biology and the relationships between biology and engineering will be transmitted to K-12 classrooms and to the general public. A fundamental theme extending throughout our education program will be "learn by doing," a method that integrates hands-on demonstrations, laboratory exercises, and classroom education with research.

The education agenda for UWEB will include graduate and undergraduate classes, a minor for graduate students that emphasizes teaching, research opportunities and summer programs for undergraduates, intern programs for under-represented groups, and summer programs for K-12 science teachers. Affiliations with the NSF ECSEL and DO-IT programs will offer additional opportunities to address undergraduate and disadvantaged students. Coordination with a strong University of Washington program, Women in Science and Engineering (WISE), will focus our efforts on introducing engineering to women. A link with the educational outreach programs of the NSF Molecular Biotechnology Science and Technology Center on our campus will permit us to tap into the K-12 science teacher training program.

An innovative UWEB research-training program will use teams called GUPIs—bench-level research groups consisting of a Graduate student, an Undergraduate student, a Professor and an Industry researcher. The function of the GUPIs is to focus research on key elements in the UWEB scientific program and to open avenues of communication among undergraduates, graduate students, professors, and industrial scientists.

An apparatus for examining the changes that occur in skin under mechanical loads (Thrust Leader, Professor Joan Sanders).

Industrial Collaboration/Technology Transfer

More than 25 companies representing the medical device and diagnostics industry are committed to UWEB. The basic agreement involves a sponsorship fee that entitles companies to participate in the program and to license UWEB technologies. To speed research in areas of corporate interest, UWEB has many options available that allow companies to invest further. UWEB will work with our corporate partners on education, recruitment, material testing, focused research, technology transfer, and program planning. Corporate affiliates will serve on our Industrial Advisory Board to provide input to UWEB organization and research planning. Industrial researchers will deepen their involvement by participating as industrial fellows, joining GUPIs, and co-supervising graduate students. Many of the corporate partners can offer our program specific biomolecules, medical devices, and equipment. These "in-kind" gifts are invaluable to the UWEB effort.

Facilities

UWEB is centrally housed in a new facility (approximately 10,000 sq. ft.) in Bagley Hall on the University of Washington campus. Special facilities include a large cell-culture laboratory for research and teaching and a cleanroom for material and device development. The facility will also house administrative offices; a classroom, conference room, and library; laboratories; and student and faculty offices. State-of-the-art surface analysis equipment is available in Benson Hall, at the University of Washington Surface Analysis Recharge Center. Each of the University of Washington investigators participating in UWEB has laboratories and research facilities, a portion of which will be oriented toward UWEB programs.

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